VERSION WITH MARKINGS TO SHOW CHANGES MADE IN THE SPECIFICATION

The change relative to the previous version, in page 13, the first paragraph is marked up as follows:

LNCaP cells, a prostate cancer cell line, were grown in RPMI 1640 medium supplemented with 2% fetal calf serum. One 70% full of cells cultured in 60mm dish were trypsinized, collected and washed three times in 5ml phosphate buffered saline (PBS, pH 7.2) at room temperature, then suspended in 1ml of ice-cold 10% formaldehyde solution in 0.15M NaCl. After one hour incubation on ice with occasional agitation, the cells were centrifuged at 13,000rpm for 2 min and wash three times in ice-cold PBS with vigorous pipetting. The collected cells were resuspended in 0.5% [Nonidet] NONIDET P40 (NP40, B.D.H.) and incubated for one hour with frequent agitation. After that, three washes were given to cells in ice-cold PBS containing 0.1M glycine and the cells were resuspended in 1ml of the same buffer with vigorous pipetting in order to be evenly separated into small aliquots and stored at -70^0C for up to a month.

REMARKS-General

1. Upon review of the original and previously amended specifications, and also in light of the observation of the Examiner noted in the above Office Action, the applicants have further amended the original specification to capitalize the trademark "NONIDET P40". No new matter has been included.

Response to Rejection of Claims 1-3, 7-18, 20, 22, 23, 25, 26, and 29-35 under 35USC112

2. Applicants acknowledge that no claims are rejected under 35 U.S.C. 102 or 103. The Examiner appears to reject the claims 1-3, 7-18, 20, 22, 23, 25, 26, and 29-35 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

3. The Examiner's rejection reason has been considered and the applicants do not found persuasive because of the following reasons:

(a) Pursuant to 35 U.S.C. 112, first paragraph, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any ***person skilled in the art*** to which it pertains, or with which it is mostly nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(b) As the Examiner notices that the specification and claims of the instant invention are recited for **person who skilled in the art of RNA library and/or the similar** to read. The applicants respectfully submit that the persons skilled in the art regarding the instant invention are those doctors who may hold a Ph.D. in biochemistry.

(c) Accordingly, the applicants strongly believe that according to the disclosure in both the specification, including the embodiments disclosed and the claims, in view of

the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims, are clear and concise for reasonable Ph.D. in biochemistry to under merit and claiming subject matters of the instant invention and to make and use the instant invention and shall set forth the best mode contemplated by the inventor of carrying out the instant invention.

4. As recited in the previous Amendment C, the nature of the present invention is related to the area of biology and chemistry, most preferably biochemistry, but not cellular physiology. Because the present invention is a combination of enzymatic reactions which are performed under an *in-vitro* (in a test tube) condition, the involvement of buffered conditions is described in detail in the examples 1-5. No workable function of the present invention is available in a living cell or by its physiology. It is understandable that an enzymatic reaction not only involves chemical kinetics but also the biological function of the enzyme(s) used. Under many *in-vitro* conditions such as *in-vitro* transcription/translation, the use of an enzymatic reaction can successfully suppress the energetic threshold of a pure chemical reaction and, therefore, provide a feasible condition for the desired reaction(s). For a better demonstration, the original claims are amended to match the step-wise description of each enzymatic step of the present invention.

5. Moreover, the relative skill of those in the art is at the same level as the referenced prior art, such as US Patent No. 5,817,465 to Mallet and No. 5,514,545 to Eberwine. A common knowledge of principal biochemistry and enzyme kinetics is required. All principal knowledge can be acquired from the referenced Sambrook's book., "*Molecular Cloning, 2nd Edition* ",Cold Spring Harbor Laboratory Press, pp8.11-8.19 (1989). Due to the fact that none of the inventors holds a Ph.D. in biochemistry, the arbitrary determination of "on par with those that hold a Ph.D. in biochemistry" is questionable.

6. Applicants believe that for all of the foregoing reasons, all of the claims 1-3, 7-18, 20, 22, 23, 25, 26, and 29-35 are in condition for allowance and such action is respectfully requested.

Respectfully submitted,

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CERTIFICATE OF MAILING

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